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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/450,880	11/29/1999	DOUGLAS A. CRAIG	56376/JPW/AD	8284

7590 06/16/2003

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/450,880	CRAIG, DOUGLAS A.	
	Examiner	Art Unit	
	Frank W Lu	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on April 18, 2002 has been entered. The claims pending in this application are claims 1-26. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Note that applicant does not address this issue.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating human urinary incontinence using compound 1 or compound 2 which can activate human 5-HT_{1F} receptor (for the name of compounds, see page 17 of the

specification), does not reasonably provide enablement for treating human urinary incontinence with any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor as recited in claims 1-26. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims 52-54 are drawn to a method of treating urinary incontinence. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001) (see below).

The Breadth of The Claims

The claims 1-24 encompass a method for treating urinary incontinence in a human subject suffering from urinary incontinence by administering to the human subject a therapeutically

effective amount of any kind of 5-HT_{1F} receptor agonist which selectively activates the human 5-5-HT_{1F} receptor.

Working Examples

The specification provides an example for treating urinary incontinence of female Sprague rats (DIRC model) using compound 1 or compound 2 (N- (N, N-Dimethyl-l, 2,3,4-tetrahydro-2-aminodibenzofur-8-yl)-pyridine-4-carboxamide or (R)-(+)-6-(4-fluorobenzoyl)amino-2-(dimethyllamino-l,2,3,4-tetrahydro-9H-carbazole).

The Amount of Direction or Guidance Provided and The State of The Prior Art

The invention relates to a method of treating urinary incontinence in human subject by administering to a human subject any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor. The specification (see pages 22-24) show that rat urinary incontinence in the DIRC model can be treated with compound 1 or compound 2 and this suggest human urinary incontinence can be treated with compound 1 or compound 2 (see applicant's declaration under 37 CFR 1.132 filed on April 29, 2002). Although the examiner agrees with applicant that 5-HT_{1F} receptor agonists are well known in the art (see page 5 of applicant's remarks filed on April 29, 2002), it is unclear whether any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor as recited in claims 1-26 can be used to treat human urinary incontinence. For example, although two 5-HT_{1F} receptor agonist, LY344864 and N-[3-(2-Dimethylaminoethyl) -2-methyl-lH-indol-5-yl]-4-fluorobenzamide can be used to treat migraine pain (see Phebus et al.,

Life Science, 61, 2117-2126, 1997 and Xu et al., J. Med. Chem., 44, 4031-4034, 2001), it is unclear whether they can be used to treat human urinary incontinence.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether a method as recited in claim 1-26 can be used to treat human urinary incontinence using any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor. As mentioned previously, since the specification does not provide a guidance s to show that any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor can be used to treat human urinary incontinence, there will be a lot of unpredictable factors when the skilled artisan uses the method recited in claim 1 to treat human urinary incontinence using any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor because it is unclear whether any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor has an ability to treat human urinary incontinence. With the predictability in the relevant art being low, the amount of experimentation needed to be exerted by the public in practicing the full scope of the invention would not fall within the limits of routine experimentation. Such efforts constitute undue experimentation. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001 (see above). As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor has an ability to treat human urinary incontinence.

Response to Arguments

In page 7, first paragraph bridging to page 11, first paragraph of applicant's remarks, applicant argues that (1) "[A]pplicant maintains that provided with the teachings of the specification, one skilled in the art of GPCR technology would recognize that it is reasonably predictable with a reasonable likelihood of success that 5-HT_{1F}-selective compounds which activate the human 5-HT_{1F} receptor can be used in the treatment of urinary incontinence."; and (2) "[A]pplicant further maintains that given the present guidance in the specification, one skilled in the art can readily obtain and identify selective 5-HT_{1F} receptor agonists that can be used to treat urinary incontinence."

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the examiner agrees with applicant that, in view of the specification, one skilled in the art can readily obtain and identify selective 5-HT_{1F} receptor agonists that can be used to treat urinary incontinence. However, the claimed invention is not directed to identify selective 5-HT_{1F} receptor agonists that can be used to treat urinary incontinence and instead the claimed invention is directed to treat urinary incontinence in a human subject by administering any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor. Because it is unclear whether any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor has an ability to treat human urinary incontinence, there will be a lot of unpredictable factors when the skilled artisan uses the method recited in claim 1 to treat human urinary incontinence using any kind of 5-HT_{1F} receptor agonist which can activate the human 5-HT_{1F} receptor. With the predictability in the relevant art being low, the amount of

experimentation needed to be exerted by the public in practicing the full scope of the invention would not fall within the limits of routine experimentation. Such efforts constitute undue experimentation.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. No claim is allowed.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94

(December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
June 4, 2003

ETHAN WHISENANT
PRIMARY EXAMINER